Review

Review of Research on Routes of Helicobacter pylori Infection

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Keywords
Helicobacter pylori, infection route, water-borne spread

Abstract
In recent years, many scholars conducted in-depth research on Helicobacter pylori and identified it as an important pathogen of chronic gastritis and peptic ulcer. H. pylori also causes and contributes to precancerous lesions (atrophic gastritis and intestinal metaplasia) and is closely related to occurrence and development of gastric adenocarcinoma and gastric mucosa-associated lymphoma. This study summarizes biological characteristics, epidemic status, and infection route of H. pylori and reviews research on roles of natural environments, especially drinking water, during infection.

In 1982, Marshall et al. [1] observed Helicobacter pylori from gastric mucosal slices and discovered a potential etiological relationship between H. pylori and gastric cancer. In recent years, many scholars performed in-depth research on H. pylori and identified it as an important pathogen of chronic gastritis and peptic ulcer. H. pylori also causes and contributes to precancerous lesions (atrophic gastritis and intestinal metaplasia) and is closely related to occurrence and development of gastric adenocarcinoma and gastric mucosa-associated lymphoma [2]. In 1994, H. pylori was listed a class I carcinogen by the International Agency for Research on Cancer [3]. This study summarizes biological characteristics, epidemic status, and infection route of H. pylori and reviews research on roles of natural environments, especially drinking water, during infection.

Biological characteristics

H. pylori is a Gram-negative bacterium with a length of 2–4 μm and width of 0.5–1 μm. This organism is also microaerophilic, suitably living at 34–40 ºC, 5%–8% O₂, 5%–10% CO₂, and high-humidity environments. Although it can survive at pH<4 acidic conditions, H. pylori can only reproduce at pH=5.5 to 8.0 [4]. H. pylori can adapt to acidic environments to a certain extent. In other words, in acidic environments, intracellular cytoplasmic pH value of H. pylori approaches neutral state. Thus, H. pylori remains capable of growth and reproduction [5] in acidic environment of gastric juices.

H. pylori is generally present in suitable environments and is spherical in shape in vitro culture, water and milk, and make contact with antibodies. This spherical type may be a self-protecting state, posing difficulty in cultivating viable bacteria [4, 6].

Epidemic status

Human H. pylori infection is prevalent worldwide. However, infection rate varies widely across the world. In some developing countries, infection rate of H. pylori can reach up to 80%, whereas in developed countries, such as the United States, infection rate totals 7.5% [7–9].

Pandeya et al. [10] surveyed 1355 adults in Australian communities using serological methods to detect H. pylori and calculated an infection rate of 15.5%. People born in Australia and New Zealand are less infected by this bacterium. Aje et al. [11] conducted a study on 46 pairs of control group with indigestion in Nigeria. Results showed higher infection rate of H. pylori (67.4%) in digestive population than that of the control group (78.3%). However, causes of such results remain unclear. Dattoli et al. [12] performed serological tests among 1104 children aged 4 to 11 years old in Salvador, Brazil and measured an infection rate of H. pylori of 28.7%. Kesanos et al. [13] researched on H. pylori infection among 101 Albanians and 101 Greeks in the Western Balkans and determined an infection rate of 54%
Infection routes of *H. pylori*

Infection routes of *H. pylori* remain unclarified. These routes may be human–human spread and environmental infection.

Human–human spread

Human–human spread results from direct contact with people and mainly occurs among families or acquaintances, such as parents and children, husband and wife, and brothers and sisters. Areas with good health conditions and low infection rate feature low probability of maternal–neonatal spread, whereas spread among siblings serves as the main route\(^\text{[9]}\). Cervantes et al.\(^\text{[20]}\) observed that *H. pylori* infection among siblings can be used as means of precaution for younger brothers and sisters, especially when age difference is less than three years old. Human–human spread can be divided into two specific forms, namely, oral–oral spread and fecal–oral spread.

Oral–oral spread

Studies on oral–oral spread showed that *H. pylori* can survive in vomit for specific periods, even reaching up to 10% survival after 24 h. As a result of vomiting or reflux, *H. pylori* can also subsist in saliva, gingiva, and plaque\(^\text{[21]}\), providing convenient conditions for oral–oral spread. Hongying et al.\(^\text{[22]}\) conducted a questionnaire survey and serological tests among 478 children in Kunming and performed logistic regression analysis (odds ratio (OR) = 2.260) and noted that shared tableware and shared toothbrush (OR = 2.094) are independent risk factors for *H. pylori* infection. Kivi et al.\(^\text{[23]}\) investigated, sampled, and identified 104 subjects among 39 families to explore specific routes of spread among family members. Results showed that in addition to mother and child, siblings and spouse can also spread bacteria through shared use of daily necessities and kisses. Zou et al.\(^\text{[24]}\) performed meta-analysis on a previous study summary and discovered significantly higher infection rate of *H. pylori* (45.0%) in mouths of people with *H. pylori* in the stomach than those without (23.9%). With drug treatment, removal rate of *H. pylori* in the stomach can reach up to 85.8%, whereas that of *H. pylori* in mouth reaches 5.7%, indicating that infection and retention of *H. pylori* in the mouth possibly serve as important route of recurrent infection in the stomach.

Some studies do not support the above view. De Sousa et al.\(^\text{[25]}\) did not find *H. pylori* population in saliva and plaque compared with *H. pylori* population in the stomach. Vale et al.\(^\text{[24]}\) also found no evidence of spread among spouses.

Fecal–oral spread

*H. pylori* can be cultured in secretions of final interception and rectum\(^\text{[27]}\); the bacterium is generally spherical in human feces and difficult to culture. However, polymerase chain reaction (PCR) can detect its DNA\(^\text{[24]}\), proving biological conditions for fecal–oral spread. Results of animal experiments support this route of spread. Cellini et al.\(^\text{[28]}\) fed 24 mice (12 infected and 12 uninfected mice) in a cage with separate compartments and fed another 24 mice (12 infected and 12 uninfected mice) in a cage without separate compartments. Results showed that mice in the cage without compartment were infected by fecal–oral spread. Oshio et al.\(^\text{[29]}\) conducted an animal experiment with gerbils and also witnessed such results. Laporte et al.\(^\text{[30]}\) conducted a cohort study in France and observed that teenagers with diarrhea in welfare houses can spread *H. pylori*, demonstrating fecal–oral spread in populations.

Drinking water and food are the main intermediate media during fecal–oral spread. Although *H. pylori* is sensitive to chlorination disinfection, tap water with chlorination disinfection does not carry live bacteria. However, local water treatment and pipe networks present significant differences. Residual chlorine concentrations of terminal...
water differ, and secondary contamination may occur. The biofilm formed by microorganisms on tap water pipe walls may also protect *H. pylori*, allowing its survival in tap water. Thus, *H. pylori* are often detected in tap water. Tap water containing residual chlorine can still be used for culture of viable bacteria after 5 min chlorination disinfection, surviving organisms presenting spherical form even after 24 h [32]. In some areas with poor water treatment and poor sanitary condition, *H. pylori* is detected in tap water [33] and is commonly found in some areas [34,35]. By contrast, *H. pylori* can survive for shorter periods in milk [36].

**Environmental infection**

Water, food, and other media containing *H. pylori* may cause *H. pylori* infection.

**Water-borne infection** *H. pylori* can survive in many water bodies. Cellini et al. [37] and Queralt et al. [38] detected *H. pylori* in marine waters, rivers, surface waters, and sewage. Viable bacteria are not easily cultured in the environment because of their spherical shape, but they can be detected by PCR. Cellini et al. [39] reported that live bacteria can be cultured in seawater samples, probably because spiral rod-shapes *H. pylori* can parasitize some microorganisms in seawater, allowing detection of this bacterium. Moreno et al. [40] used improved membrane separation and enrichment techniques and fluorescence in situ hybridization to successfully culture viable bacteria, providing new evidence for environmental infection. Many studies on population epidemiology confirmed infection routes of *H. pylori*. Xiaojing et al. [41] investigated and detected 1127 subjects in Guizhou Province and used logistic regression and respectively observed significantly higher positive rates (64.2% and 36.6%) of anti-Hp-IgG and IgM of people drinking river water than those drinking tap water (50.6% and 27.3%) and well water (57.3% and 28.1%). Lihua et al. [42] conducted investigations, sampling, and detection among 938 children and teenagers aged 3 to 18 years old in Gan Su and noted significantly higher infection rate of those drinking river water (78.1%) and well water (75.9%) than that those consuming tap water (68.1%). Tianzhe et al. [43] conducted a meta-analysis on previous research literature and discovered that drinking water habits are mostly correlated with *H. pylori* infection. Drinking unboiled water (OR = 3.08, 95% confidence interval (CI) = 1.02–9.26) and unclean water (OR = 2.01, 95% CI=1.35–3.00) is also an independent risk factor for infection.

**Infection from food** Few studies reported food infections. Papeix et al. [44] observed that infection rate of *H. pylori* in shepherds reaches as high as 97.6% among Polish people. This value is much higher than that of the general population (65.1%). Quaglia et al. [36] indicated that *H. pylori* can survive in goat’s milk for some time, and shepherds may be infected by drinking goat’s milk. Some researchers reported that raw vegetables and meat can also increase risk of infection.

**Conclusion**

Various epidemiological studies showed that environmental mediators are important sources of *H. pylori* infection and feature significance to economic development and public health. However, no direct evidence shows that *H. pylori* can infect populations through environmental mediators. As a result of its biological characteristics, difficulty arises from culturing viable *H. pylori* in environmental samples. Results of PCR detection provide insufficient direct evidence. Thus, infection routes remain controversial. Recently, Moreno et al. [40] cultured viable bacteria obtained in sewage. When this method is successfully used in other environmental samples, it will serve as an important culturing method for *H. pylori*; although curative rate of *H. pylori* with drug treatment approximates 80% (slightly different according to strain virulence and drug resistance), recurrence rate is also high, and developing countries exhibit significantly higher yearly recurrence rate (13%) than developed countries (2.67%) [45-47]. In-depth studies covered the use of epidemiology, genomics, animal models, and other means to explore direct evidence of environmental infection routes of *H. pylori* and to conduct risk assessment of environmental infection and pathogenicity; these research will provide scientific basis for development of public health policies that guide clinical treatment and intervening risk factors and solid foundation for effective prevention and treatment of *H. pylori* infection and diseases.

**Declarations**

**Acknowledgements**

No.

**Competing interests**

The author declare that he has no competing interest.
**Authors' contributions**

H Li made the literature analysis and wrote, discussed and revised the manuscript of this review.

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